Table A.30 Withdrawal due to lack of Arthritis Efficacy (060, 087)

BC-58635 QD VS BID EFFICACY IN KNEE OA M49-96-02-060

INCIDENCE OF WITHDRAWAL DUE TO LACK OF ARTHRITIS EFFICACY

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO	9C-58635 100MG BID	8C-58635
	(第=231)	(N=231)	200MG QD (N=222)
NUMBER WITHDRAWN DUE TO LACK OF ARTHRITIS EFFICACY	56 (24%)	18(8%)	21(9%)
p-VALUES FOR OVERALL COMPARISONS (a):	<0.001		
p-values for treatment comparisons (b):			
	100MG BID VS.	200MG QD Vs.	200mg QD Vs.
	PLACEBO	PLACEBO	100MG BID
	<0.001	<0.001	0.616

SC-98635 QD VS BID EFFICACY IN KNEE GA M49 98 02 087

TABLE 20

INCIDENCE OF WITHDRAWAL DUE TO LACK OF ARTHRITIS EFFICACY

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO	SC-58635 100 % 3 RTD	SC-58635 LBOMG OD
	(N=243)	(N=241)	'N=2 (1)
NUMBER WITHDRAWN DUE TO LACK OF ARTHRITIS EFFICACY	55 (23%)	27(114)	24(10%)
p VALUES FOR CVERALL COMPANISORS (a):			
p-Values for treatment comparisons (b):			
	100MG BID URL	200 m s QD Vs.	200MG QD Vs.
	FLAJEBS	PLACEBO	100MG BIC
	45.701	<0.001	5 882

⁽a) Fisher's Exact test

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⁽a) Fisher's Exact test
(b) Pairwise Fisher's Exact test

⁽b) Pairwise Fusher's Exact test

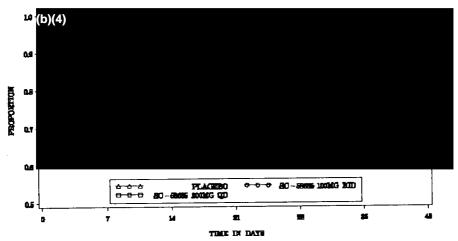
Table A.31 Time to Withdrawal-Lack of Arthritis Efficacy (060, 087)

80-9866 QD V8 200 EFFEMOT DE ENEM CA NOV-98-98-98

TANT P 99

TIME TO WITHDRAWAL DUE TO LACK OF ARTHRITIS EFFICACY
FART I OF & MAPLAN - MCDICR ESTIMATES OF PROPORTION OF PATIENTS
WHO DID NOT WITHDRAW DUE TO LACK OF ARTHRITIS REFICACY

DITENT-TO-TERAT COHORT (TT)



SC-58685 QD V8 BID EFFICACY IN KNEE OA N48-98-02-087

TABLE 21

TIME TO WITHDRAWAL DUE TO LACK OF ARTHRITIS EFFICACY PART 1 OF 2: KAPLAN - MEIER ESTIMATES OF PROPORTION OF PATTENTS WHO DID NOT WITHDRAW DUE TO LACK OF ARTHRITIS EFFICACY

INTENT-TO-TREAT COHORT (ITT)

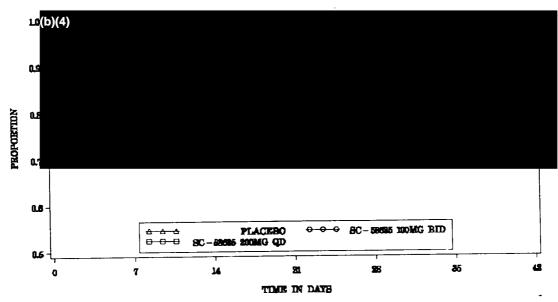


Table A.32 Schedule of Observations and Procedures (protocol 022)

	Screening Visit -7 to -2 day	Baseline Visit (Day 0)	Week 2 (Day 14) (_1 day)	Week 5 (Day 42) (_3 days)	Week 12 (Day 84) (_5 days)	Early Termina- tion
informed Consent	Х					
Medical History	Х					
Physical Examination	Х				Х	Х
Clinical laboratory tests (a)	Х		X	X (b)	×	Х
Discontinue NSAID (c)	Х					,
Meet Flare Criteria		X		<u> </u>		
C-Reactive Protein		Х	Х	х	Х	X
Rheumatoid Factor	х					- · · · · · · · · · · · · · · · · · · ·
SF-36 Health Survey		Х			Х	Х
Health Assessment Questionnaire (HAQ)		Х	×	×	х	Х
RA Assessments	X (d)	X	X	Х	Х	Х
UGI Endoscopy	X (e)				Х	X
Signs and Symptoms		Х	Х	Х	Х	Х
Dispense Study Medication		x	x ,	×		
Return and Count Study Medication			х	×	х	×
Dispense Concurrent Meds Diary Card		Х	×	х		
Collect Concurrent Meds Diary Card			х	х	х	Х

- (a) Clinical laboratory tests included **Hematology** (white blood cell [WBC] count with differential, red blood cell [RBC] count, hemoglobin, hematocrit, platelet count [estimate not acceptable], prothrombin time [PT], and partial thromboplastin time [PTT]); **Biochemistry** (sodium, potassium, chloride, calcium, inorganic phosphorus, blood urea nitrogen [BUN], creatinine, total protein, albumin, total bilirubin, uric acid, glucose, alkaline phosphatase, AST [SGOT], ALT [SGPT], creatine kinase [CK]); and **Urinalysis** (pH, specific gravity, WBC, RBC, protein, glucose, ketones, bilirubin). FlexSure① (Baseline) and CLOtest at Final Visit for H. pylori. Serum pregnancy test was performed within seven days before Baseline Arthritis Assessments for women of childbearing potential.
- (b) PT and PTT were not performed at the Week 6 Visit.
- (c) Patients discontinued oxaprozin and/or piroxicam at least four days before the Baseline Arthritic Assessments.
- (d) Screening arthritis assessment data were collected by Searle but not entered into the database.
- (e) Pretreatment (Baseline) endoscopy must have been performed within seven days before the first dose of study medication.

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Table A.33 Baseline demographics (study 022, 023-pooled)

Text Table 44. Pooled Baseline Demographic Characteristics and Disease Status for RA Patients By Treatment Group (All Randomized Patients: Pooled Pivotal Studies 022 and 023)

		Number of Pa	atients by Trea	tment Group	
				Naproxen	
	Placebo	100 mg BiD	200 mg BID	400 mg BID	500 mg BIC
Baseline Characteristic	(n≃452)	(n=468)	(n=454 °)	(n=435 °)	(n=443)
Age (years)					
Mean (Std. Dev.)	54.2 (12.42)	55.1 (11.99)	54.0 (12.09)	54.0 (12.10)	55.9 (12.09
Ran ge	(b)(4)				
<65 years - N (%)	350 (77%)	364 (78%)	351 (77%)	344 (79%)	321 (72%)
265 years - N (%)	102 (23%)	104 (22%)	103 (23%)	91 (21%)	122 (28%)
Race/Ethnic Origin					
Asian - N (%)	1 (<1%)	4 (<1%)	6 (1%)	4 (<1%)	1 (<1%)
Black - N (%)	36 (8%)	42 (9%)	35 (8%)	35 (8%)	34 (8%)
Caucasian - N (%)	391 (87%)	394 (84%)	380 (84%)	364 (84%)	377 (85%)
Hispanic - N (%)	23 (5%)	25 (5%)	32 (7%)	28 (6%)	28 (6%)
Other - N (%)	1 (<1%)	3 (<1%)	1 (<1%)	4 (<1%)	3 (<1%
Gender					
Female - N (%)	336 (74%)	346 (74%)	328 (72%)	314 (72%)	313 (71%)
Male - N (%)	116 (26%)	122 (26%)	126 (28%)	121 (28%)	130 (29%
Disease Duration - Years				İ	1
Mean (Std. Dev.)	10.3 (±9.91)	10.7 (±9.01)	10.4 (±9.32)	10.3 (±8.77)	11.0 (=9.80
Range	0.3-60.0	0.3-53.0	0.3-53.0	0.3-58.0	0.3-55.0
<5 years - N (%)	159 (35%)	135 (29%)	166 (37%)	150 (34%)	143 (32%
≥5 years · N (%)	293 (65%)	333 (71%)	288 (63%)	285 (66%)	300 (68%
Corticosteroid Use			1	ļ	
Yes - N (%)	175 (39%)	209 (45%)	172 (38%)	154 (35%)	167 (38%
No - N (%)	277 (61%)	259 (55%)	282 (62%)	281 (65%)	276 (62%
Methotrexate Use			Ì	Į	
Yes - N (%)	192 (42%)	221 (47%)	205 (45%)	202 (46%)	200 (45%
No - N (%)	260 (58%)	247 (53%)	249 (55%)	233 (54%)	243 (55%
Other DMARD Use					1
Yes - N (%)	148 (33%)	153 (33%)	139 (31%)	132 (30%)	149 (34%
No - N (%)	304 (67%)	315 (67%)	315 (69%)	303 (70%)	294 (66%

Pooled Pivotal Studies 022 and 023)

1 0010	u Protai Studic									
		Number of Patients by Treatment Group								
			Celecoxib		Naproxen					
	Placebo	100 mg BID	200 mg BID	400 mg BID	500 mg BID					
Baseline Measure	(n=452)	(n⇔468)	(n=454 °)	(n=435 °)	(n=443)					
Patient's Global Assessme	ent of Arthritic Con-	dition - N (%)								
Very Good	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)					
Good	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)					
Fair	169 (37%)	181 (39%)	184 (41%)	175 (40%)	189 (43%)					
Poor	227 (50%)	230 (49%)	212 (47%)	204 (47%)	209 (47%)					
Very Poor	56 (12%)	57 (12%)	58 (13%)	56 (13%)	45 (10%)					
Number of Tender/Painful	Joints									
Mean (Std. Dev.)	28.7 (14.55)	28.2 (14.40)	29.6 (14.99)	28.8 (14.36)	28.2 (14.01)					
Range	(b)(4)									
Number of Swollen Joints										
Mean (Std. Dev.)	20.9 (11.83)	20.5 (11.68)	21.7 (12.29)	20.7 (11.80)	20.6 (12.11)					
Range	(b)(4)									
Physician's Global Assess	sment of Altunius C	Oliginion - It I	• /							
Very Good	0 (0°c)	0 (0°°)	0 (0°≈)	0 (0%)	0 (0%)					
Good	C (C*=)	1 (<1%a)	0 (0%)	0 (0%)	0 (0%)					
Fair	199 (44%)	207 (44%)	183 (40%)	182 (42%)	191 (43%)					
Poor	220 (49 ⁶ s)	218 (47%)	227 (50%)	216 (50%)	219 (50%)					
Very Poor	33 (7%)	42 (9%)	44 (10%)	37 (9%)	32 (7%)					

Table A.34.1 Physician's Global Assessment (Protocol 023)

TABLE 20 PHYSICIAN'S GLOBAL ASSESSMENT OF ARTHRITIS PART 1 OF 4: OBSERVED MEANS (a) (b)

. *		INTENT-TO-TREAT COHORT (ITT)							
	PLACEBO	SC-58635 100MG BID	8C-58635 200MG BID	8C-58635 400MG NID	NAPROXEN 500MG BID				
	(M=221)	(N=228)	(M+218)	(M=217)	(M=218)				
BASELINE									
N	221	228	218	217	218				
MEAN	3.6	3.7	3.7	3.7	3.7				
STD DEV	0.61	0.65	0.64	0.62	0.63				
WEEK 2									
W	221	228	218	217	218				
MEAN	3.3	2.9	2.7	2.8	2.7				
STD DEV	0.90	0.86	0.84	0.00	0.82				
WEEK 6									
Ħ	221	228	210	217	218				
MEAN	3.2	2.9	2.8	2.8	2.7				
STD DEV	1.01	0.93	0.95	0.91	0.87				
WEEK 12									
N	221	228	218	217	218				
MEAN	3.3	3.0	2.9	2.0	2.8				
STD DEV	1.00	0.95	0.93	0.92	0.92				

(a) This table is based on the last observation carried forward approach

PHYSICIAN'S GLOBAL ASSESSMENT OF ARTHRITIS PART 2 OF 41 CATEGORICAL CHANGE ANALYSIS, MUNBER OF PATIENTS (%) (a)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO	SC-58635 100MG BID	SC-58635 200MG BID	9C+58635 400MG BID	MAPROXEN 500MG BID	LINEAR TREND
	(N=221)	(N=228)	(M=218)	(M=217)	(N=218)	D-AYTAE (q)
WEEK 2						<0.001
IMPROVED (b)	22(10%)	44(19%)	60 (28%)	46(21%)	55(25%)	
NO CHANGE	187 (85%)	179(79%)	151(69%)	171(79%)	161(74%)	
WORSENED (c)	12(5%)	5(2%)	7(3%)	0(0%)	2(<1%)	
TOTAL	221(100%)	228(100%)	218(100%)	217 (100%)	218(100%)	
NEEK 6						0.009
IMPROVED (b)	30(14%)	42(18%)	54 (25%)	39(18%)	52(24%)	
NO CHANGE	177(80%)	178 (78%)	158(72%)	177(02%)	164(75%)	
WORSTENIED (c)	14(6%)	8 (4%)	6(3%)	1(<1%)	2(<1%)	
TOTAL	221(100%)	228(100%)	218(100%)	217 (100%)	218(100%)	
WEEK 12						0.001
IMPROVED (b)	27(12%)	42(18%)	48(22%)	44(20%)	55(25%)	
NO CHANGE	178(81%)	179(79%)	164(75%)	171(79%)	160(73%)	
WORSENED (c)	16(7%)	7 (3%)	6(-3%)	2(<1%)	3(1%)	
TOTAL.	221(100%)	220(100%)	218(100%)	217 (100%)	218(100%)	

p-values for treatment comparisons (e) :

							-SECONDARY			
	200MG BID Vs. PLACEBO	400MG BID VS. PLACEBO	100MG BID VS. PLACEBO		400MG BID Vs. 100MG BID	VS.	vs.	NAPROXEN VS. 100MG BID	VS. 200MG BID	NAPROXEN V9. 400MG BID
WEEK 2: WEEK 6: WEEK 12:	<0.001* 0.001* 0.003*	<0.001* 0.016* 0.001*	<0.001 0.035 0.004	0.120 0.115 0.410	0.423 0.753 0.681	0.284 C.181 0.820	<0.001 <0.001 <0.001	0.097 0.109 0.096	0.931 0.885 0.285	0.273 0.156 0.22 9

 ⁽b) Scale ranged from 1 (very good) to 5 (very poor)
 By definition, in this and subsequent efficacy tables, the ITT cohort includes only patients who had at least one dose of study medication

⁽a) This table is based on the last observation carried forward approach

(b) Improved is defined as reduction of at least two grades from baseline for grades 3-5 or a change in grade from 2 to 1

(c) Worsened is defined as an increase of at least two grades from baseline for grades 1-3 or a change in grade from 4 to 5

(d) Cochran-Mantel-Haenszel test of linear dose trend stratified by center (Nonzero Correlation), Maproxen group was excluded

(e) Cochran-Mantel-Haenszel test of treatment comparison stratified by center (Row Mean Scores Differ)

* Statistically significant according to the Hochberg procedure (primary pairwise comparisons only)

Table A.34.2 Physician's Global Assessment-continued (Protocol 023)

PHYSICIAN'S GLOSAL ASSESSMENT OF ARTHRITIS PART 3 OF 4: MEAN CHANGE AMALYSIS (a) (b) INTENT-TO-THEAT COMORT (ITT)

	PLACEBO (N=221)	8C-58635 100MG BID (N=228)	200MG BID			OVERALL p-VALUE(c)	LIMEAR TREND p-VALUE(d)
						<0.001	<0.001
WEEK 2						40.001	40.001
OBSERVED MEAN CHANGE	-0.4			-0.9	0.90		
STD DEV			0.93				
LB MEAN CHANGE (c)	-0.3	-0.8	-1.0	-0.9	-1.0		
WEEK 6						<0.001	<0.001
OBSERVED MEAN CHANGE	-0-4	-0.7	-0.9	-0.9	-1.0		
STD DEV	0.96	0.96	1.03	0.89	0.95	*	
LS MEAN CHANGE (c)	-0.4	-0.7	-0.B	-0.B	-0.9		
						<0.001	<0.001
WEEK 12 OBSERVED MEAN CHANGE	-0.3	-0.7	-0 B	-0.8	-0.9	-	
				0.92			
STD DEV LE NEAN CHANGE (c)	-0.3		-0.8				
ES NEXA CHIDIOL (C)							
Q-RATIO WITH 95% CONFIDENCE INTERVA	LS (•): 100m	G BID VS. MA	PROXEN	200MG BID VS.	NAPROXEN	400MG BID	S. NAPROXES
WREK 2:	0.7	8 (0.65 to	0.93)	0.98 (0.83 (20 1.15)	0.89 (0.1	75 to 1.05)
WEEK 6:				0.89 (0.73 1			
WEEK 12:				0.88 (0.71 1			
p-values for treatment comparisons	(f):						
PRIMARY	1			-SECOMDARY			
200MG BID 400MG BID	100MG BID 2001	G BID 400MG	BID 400967	BID MAPROXE	NAPROXEN VS.	naproxem	HAPROXEN VS.
PLACEBO PLACEBO	PLACEBO 1000	BID 10030		BID PLACEBO	100MG BI		400MG BID

	PRI	MARY				8200	edary			
	ZOOMG BID	,		200MG BID Vs.	400MG BID VE.	400MG BID V9.	MAPROXEM VB.	Naproxen VS.	NAPROXEM VS.	NAPROXEN VS.
	PLACEBO	PLACEBO	PLACEBO	100MG BID	100MG BID	200MG BID	PLACEBO	100MG BID	200MG BID	400MG BID
WEEK 2:	<0.001*	<0.001*	<0.001	0.009	0.154	0.244	<0.001	0.004	0.790	0.153
WEEK 6:	<0.001*	<0.001*	<0.001	0.113	0.121	0.972	<0.001	0.004	0.205	0.193
WREK 12:	<0.001*	<0.001*	<0.001	0.135	0.070	0.750	<0.001	0.005	0.199	0.334

⁽a) This table is based on the last observation carried forward approach
(b) Scale ranged from 1 (very good) to 5 (very poor) with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and Baseline value as covariate,
the corresponding ROOT MSE are: 0.787 for weak 2, 0.868 for weak 6, 0.883 for weak 12
(d) From a contrast statement from Analysis of Covariance model in (c), Naproxem group was excluded
(e) Q-RATIO is defined as the ratio of least square meen changes from (c), of SC-58635 group versus Maproxem group
(f) From a contrast statement from Analysis of Covariance model in (c)

* Statistically significant according to the Bochberg procedure(primary pairwise comparisons only)

Table A.35.1 Patient's Global Assessment (Protocol 023)

TABLE 17 PATIENT'S GLOBAL ASSESSMENT OF ARTHRITIS PART 1 OF 4: OBSERVED MEANS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (N=221)	8C-58635 100MG BID (N=228)	SC-58635 200MG BID (Me218)	SC-58635 400MG BID (N=217)	MAPROXEM 500MG BID (N=218)
BASELINE					
¥	221	228	218	217	218
MEAN	3.7	3.7	3.7	3.1	3.7
STD DEV	0.68	0.67	0.66	0.54	0.63
WEEK 2					
H	271	228	218	217	218
MEAN	3.4	2.9	2.7	2.7	2.7
STD DEV	0.96	0.90	0.88	0.62	0.03
MEEK 6					
8	221	228	218	217	218
HOBAN	3.4	3.0	2.8	2.9	2.0
STD DEV	1.04	0.96	1.00	0.96	0.94
WEEK 12					
M	221	228	219	217	210
MEAN	3.4	3.1	2.9	3.0	2.8
STO DEV	1.05	0.98	0.98	0.92	0.94

PATIENT'S GLOBAL ASSESSMENT OF ARTHRITIS PART 2 OF 4: CATEGORICAL CHANGE ANALYSIS, NUMBER OF PATIENTS (%) (m)

INTENT-TO-TREAT CORORT (ITT)

	PLACEBO	BC-58635 100MG BID	SC-58635 200MG BID	SC-58635 400MG BID	HAPROXEN 500MG BID	LIMEAR TREND
•	(M=221)	(N=228)	(M=218)	(M=217)	(N=218)	p-Value (d)
						<0.001
WEEK 2	24(11%)	49(21%)	\$4 (25%)	61(28%)	61(28%)	
IMPROVED (b)	183(83%)	174 (76%)	158(72%)	152 (70%)	154 (71%)	
NO CHANGE		5(2%)	6(3%)	4(2%)	3(1%)	
WORSENED (c)	14(6%)	31 24/	U () U)	41/	3, 2-,	
	221(100%)	228 (100%)	218(100%)	217 (100%)	218(100%)	
TOTAL	211(1004)	220(1004)	22012000,			
						0.001
WEEK 6	27(12%)	44(19%)	54(25%)	45(21%)	53(24%)	
IMPROVED (b)	176(80%)	177(78%)	156(72%)		160(73%)	
NO CHANGE			8(4%)	4(2%)	5(2%)	
MORSERED (c)	18(8%)	7 (3%)	W(44)	4(24)	3(24)	
	221(100%)	228 (100%)	218(100%)	217 (100%)	218(100%)	
TOTAL	221(1004)	220(2000)				
WEEK 12						0.007
	29(13%)	40(18%)	50(23%)	41(19%)	57(26%)	
IMPROVED (b)	171 (77%)		160(73%)	169 (78%)	157(72%)	
NO CHANGE	21(10%)	8(45)	E(4%)	7 (3%)	4 (2%)	
WORSENED (c)	21(100)		-, -,	.,,		
	221(100%)	220(100%)	218(100%)	217(100%)	218(100%)	
TOTAL	221,2004,					

p-values for treatment comparisons (*) :

	PRI	MARY	\			SECC	MINARY			
	200MG BID Vs. PLACEBO	400MG BID VS. PLACEBO	100MG BID VS. PLACEBO	200MG BID Vs.	400MG BID VS.	400MG BID	NAPROXEN VS	VS. 10CMG BID	VS.	VS.
WEEK 2: WEEK 6: WEEK 12:	<0.001* 6.061* 0.002*	<0.001° 0.001° 0.007°	<0.001 0.004 0.016	0.688 0.374 0.294	0.171 0.742 0.813	0.335 0.618 0.411	<0.001 <0.001 <0.001	0.099 0.217 0.026	0.352 0.828 0.302	0.959 0.371 0.063

 ⁽a) This table is based on the last observation carried forward approach
 (b) Scale ranged from 1 (very good) to 5 (very poor)
 By definition, in this and subsequent efficacy tables, the ITT cohort includes only patients who had at least one dose of study medication

⁽a) This table is based on the last observation carried forward approach
(b) Improved is defined as reduction of at least two grades from baseline for grades 3-5 or a change in grade from 2 to 1
(c) Morsaned is defined as an increase of at least two grades from baseline for grades 1-3 or a change in grade from 4 to 5
(d) Cochran-Mantel-Maensrel test of linear dose trend stratified by center (Monzero Correlation), Magroxen group was excluded
(e) Cochran-Mantel-Maensrel test of treatment comparison stratified by center (Row Mean Scores Differ)

* Statistically significant according to the Bochberg procedure (primary pairwise comparisons only)

Table A.35.2 Patient's Global Assessment-continued (Protocol 023)

TABLE 17 PATIENT'S GLOBAL ASSESSMENT OF ARTHRITIS PART 3 OF 4: MEAN CHANCE ANALYSIS (a) (b) INTENT-TO-TREAT COHORT (ITT)

	PLACEBO	6C-50635 100MG BID		400MG BID	MAPROXEN 500MG BID	OVERALL	LINEAR TREND
	(H=221)	(N=228)	(N=218)	(N=217)	(N=218)	p-VALUE(c)	p-VALUE(d)
WREK 2						<0.001	<0.001
OBSERVED MEAN CHANGE	-0.4	-0.8	-1.0				
STD DEV	0.93	0.99	0.90	0.90	0.91		
LE MEAN CHANGE (c)	-0.3	-0.0	-1.0	-1.0	-1.0		
MORCEN 6						<0.001	<0.001
OBSERVED NEAN CHANGE	-0.4	-0.7	-0.8	-0.8	-0.9	•	
STD DEV	0.96	0.99	1.04	0.95	0.99		
LS MEAN CHANGE (c)	-0.3	-0.7	-0.8	-0. B	-0.9		
WREK 12						<0.001	<0.001
OBSERVED MEAN CHANGE	-0.3	-0.6	-0.8	-0.7	-0.9		
STD DEV	0.97	0.97	1.01	0.96	1.00		
LS MEAN CHANGE (c)	-0.3	-0.6	-0.8	-0.7	-0.9		
Q-RATIO WITH 95% CONFIDENCE INTERVA	LS (*): 100m	M BID VS. NA	PROXEN 2	OONG BID VS. N	iaproxen	400MO BID V	S. NAPROXEN
WREK 2:	0.7	8 (0.64 to	0.93}	0.95 (0.81 ta	1.12)	0.94 (0.8	10 to 1.11)
WREK 6:				0.92 (0.74 to			0 to 1.08)
WEEK 12:	0.6	6 (0.50 to	0.86)	0.89 (0.71 to	1.12)	0.82 (0.6	55 to 1.04)
p-values for treatment comparisons	(£) i						
PRIMARY	1			FECONDARY			
200MG BID 409MG BID Vs. Vs.	100MG BID 200M	IG BID 400MG	BID 400MG 1 . VS. BID 200M2 1	BID MAPROXEN Vs. BID PLACEBO	NAPROXEN V8. 100MG BID	VS. 200MG BID	VS. 400MG BID
		24 0.03		<0.001	0.004	0.548	0.478
WREK 2: <0.001* <0.001* WREK 6: <0.001* <0.001*				<0.001		0.405	0.201
		124 0.12		<0.001		0.304	0.083

WEEK 6: WEEK 12: <0.001* 0.001

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 1 (very good) to 5 (very poor) with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and Baseline value as covariate,
the corresponding ROOT MSE are: 0.826 for week 2, 0.914 for week 6, 0.909 for week 12
(d) From a contrast statement from Analysis of Covariance model in (c), Naproxem group was excluded
(e) Q-RATIO is defined as the ratio of least square mean changes from (c), of SC-58635 group versus Naproxem group
(f) From a contrast statement from Analysis of Covariance model in (c)

* Statistically significant according to the Nochberg procedure(primary pairwise comparisons only)

Table A.36.1 Number of Tender/Painful Joints (Protocol 022)

346 56 02 322

TABLE 20 NUMBER OF TENDEN PAINFUL COINTS PART 1 OF 50 DESPRIED MEANS (4) (6)

STOL CAMEND CARREST OF CARREST

	PLACERO	50-58635 100MG 61D	50-54615 10.M3 BID	57-58645 400N3 61D	NAPROXEN SOOMS BID
	(N 231)	(N-240)	(N 235)	C+ 117)	(N 225)
DASDLINE					
20	231	249	235	217	225
REAN	29.7	29.6	31.0	28.2 .	28.3
STO DEV	14.85	54.94	15.24	14.31	14.27
WEEK C					
N	Z3 I	040	235	217	225
MEAN	21.8	18.5	18.8	7.K.A	1.6.0
ALD DELY	15.43	10.19	15.77	14.35	15.20
WEEK 6					
24	231	240	235	217	225
MEAN	30.⊁	<u>1</u> #.5	18.7	16.5	18.2
STO DEV	16,85	16.39	15.71	14,59	15.35
MEER 12					
N	2 +1	240	235	217	225
MEAN	21.1	17.9	18.6	16.5	18.6
WID DEW	17,27	16.04	1G.24	14.95	16.06

(a) This table is based on the last observation carried forward approach () doubt ranged from 0 to 00 with lower econe as bester

MAZZER OF THEORY FAMILIES OF THEORY FAMILY COURTS.

HAST I HE THE SATIENT'S OFFRALL STATUS IN CHANGE FROM SASELINE, NOMBER OF PATIENTS (N) (4)

INTENT OU PREAT COMPUNE (1771)

	PLAK.EBO	86-79635 190MG BID	90-58635 200mg bid	20-58635 400MG BED	NAPROXEN SCOMU BID	LINEAR TREND
	(M 231)	(N. 240)	(N 235)	(N: 217)	(N-225)	p-VALUE (d)
WEEK 2						0.001
1MPROVED (b)	72: 31%)	194 (43%)	112(48%)	103 (47%)	195(47%)	
NG CHANGE	148 (648)	1297 54%3	115 (49%)	108 (50%)	132(50%)	
WORSENED (n)	11(56)	7 (35)	2 (3%)	6(31)	6(4%)	
TOTAL	231 (1994)	240 (100%)	235 (100%)	217 (100%)	225 (100%)	
WEEK G						0.004
IMPROVED (b)	89(39%)	1161 4931	108 (45%)	109(50%)	108(48%)	
NG CHANGE	126(55%)	107(45%)	1221 53%1	104(48%	105(47%)	
WORSERED (c)	15: 7%)	15(61)	51 2%;	4(2%)	12(51)	
79.7% <u>1</u>	201:17(*)	740(196%)	235 (100%)	227(100%)	225(100%)	
super 10						3.614
IMPROVED DO	#81 3893	2277 53%)	1151 49*1	104(48%)	98(44%)	
NO CHANGE	1981 55 8 .	96 (46%)	100.1 40%	195 (48%)	132(50%)	
WORSEMED (F)	101 -31	721 361	#1 3%)	8(4%)	15(7%)	
TOTAL:	2 (1) 1 / 2 (1)	.407100%.	7 tf t180*1	217(100%)	225(100%)	

g WALDER DE LEBATRETH COMPLETE ONE OF CO.

		M7 5	SECONDARY									
) 1681 But 701	anders established established	10 18 × 810 10 ×	I has alb	.00 4 0 €10 ₩2.	46963 BIB VS.	NAFROXEN VS.	nappoxén Vs. Jagne byd	naproxen VS	KAPFOXER VS.		
645E: 23	9.395	3.1511	1.061	1 314	0.277	0.945	0.001	0.549	0.682	0.733		
31 EN 43	1	Secretary *	1.617	.,564	0.497	C.47.d	0.031	0.785	0.763	೦.656		
WEEK 14:		0.016*	1.902	1.781	0.761	6.754	0.225	0.091	0.195	0.264		

⁽a) This taken to lead on the last observation furtial forward approach

in Tage two is distinct as common of improved joints minus number of borsoned joints is larger than or expert to bow or
the number of joints with baseline source x 5

(Workened is defined as number of expected indice minus number of interest office in larger than or equal to 50% of
the number of joints with baseline source x 0

(d) Tochsan-Mantel-Happroach test of linear doze trend stratified by denier Monroe Cortelation, Naprikes group was excluded
to Forman Mantel Expensed test of treatment composition stratified by tester about the number of inferior
to restrictionly significant as origing to the Successful processor, as which improve the

Table A.36.2 Number of Tender/Painful Joints-(Protocol 022)

PART 3 OF 5 MEAN DRAWE ANALYSIS (8) (6) INTENT-THIRAT CORDST (ITT)

			PLATE	-	100MA FIR	20-58635 200MG_BID	400MC RID	MOOMG RID	OVERALL p-VALUE(c)	
			.N=27	1 .	(N=243)	(N=235)	(N=217)	(M=225)	p-valua (c)	p-value (a)
									4.0.60t	<6.061
GEN D			_^.		-11.1	228.5	-11.3	-16.2		
	MERCH CHANGE				12.3*	11.77	11.66			
SIT DEV					1111		-12.6		•	
13 MEANS	HDM (E. Co.)									
									0.004	<0.001
1887 ·				č.	411.1	-11.3	+11.17	-1000		
	MEAN HADIE			7.6	12.16	11.05	12.84	12.55		
TID DEY			- 1		-11.1		-12	-1		
LS MISAN C	HANGD (d)			-						
									-0.001	<0.001
FFY 11				£.	235 B	-12-4	-11.7	-9.5		
	MEAN CHANGE		141		14.14	13.99	13,59	11.16		
SID DEV					-12.0		-15.4	-16.1		
LA MEAN V	HAMSE (c)									
RATIO RII	H 95% CONFLD	ENCE INTERV	ALS (e):	100M0	BID VS. NA	PECKEM	200ms BID VS.	HAPROXYN	400Mg BID V	S. NAPHOX
							1.11 (0.92	** 1 341	1.11 (0.9	o e - 1 30
				1.05	. 1 3 67 56		しょうきょう しんりょうかい			
	WEEK 2:					- 6/-	4 40 7 6 60	to 3 401	3 16 (6) 5	
	WEER 6:			1.07	1 0.87 to	1.33)	1.13 (8.92	to 1,40)	1.16 (0.3	4 to 1.4
				1.07	1 0.87 to	1.33)	1.13 (8.92 1.22 (8.98	to 1,40)	1.16 (0.5 1.23 (0.5	4 to 1.4
. W.E.* 1172 O F1/	WEEK 6: WEEK 12:	mrwpasiscks	:51:	1.07	1 0.87 to	1.33)	1.13 (8.92	to 1,40)		4 to 1.4
-VALUES FO	WEER 6: WEEK 12: OR TREATMONT			1.09	(0.87 to	1.33) 1.49)	1.13 (0.92 1.22 (0.98	to 1.40) to 1.52)	1.23 (0.5	4 to 1.4.
PRESIDENT	WEER 5: WEEK 12: OR TREATMENT	Mar Dati		1,00	(0.87 to (0.96 to	1.33)	1.13 (8.92 1.22 (8.98	to 1.40) to 1.52)	1.23 (0.5	4 to 1.4
-VALUES FO	WEER 5: WEEK 12: OR TREATMENT	MARY: &ACMA RID	THE CM TO	1.00 1.19	(0.87 to (0.96 to	1.33) 1.49)	1.13 (8.92 1.22 (8.98 SECUNDARY	to 1.40) to 1.52) EN NAPROXEN	1.23 (0.5	A to 1.4 P9 to 1.5 NAPROXEN
-VALUES FO	WEER 5: WEEK 12: OR TREATMENT	MARY: I GACMA BID	378 785 P1	1.03 1.35	0.87 to	1.33) 1.49)	1.13 (8.92 1.22 (8.98 SECUNDARY	to 1.40) to 1.52) FR NAPROXEN VS.	1.23 (0.5 NAPROXEN VS.	MAPROXEN VS.
-VALUES FO	WEER 6: WEEK 12: OR TREATMENT	MARY: I 450MA RID VX PEACEA.	CHIMA BID ME. PLANSEN	1.03 1.19 207 M	1 0.87 to 1 0.96 to 2 1 812 405MC	1.33) 1.49) : RTD 400MG : VE : SED 200MG	1.13 (8.92 1.22 (0.98 -SECONDARY ETD NAFROXE VE. VE.	E0 1.40) E0 1.52) FM NAPROXEN VS. 7 180MG ST	2.0) £5.1 NAKORGAN 2V COTE ONODE O	MAPROXEN VS. 40 to 1.5
	WEER 6: WEEK 12: OR TREATMONT 	MARY: : 4ACHA BID VX PEACBB.	CHIMA BID NY. PLANCEN	1.03 1.35 257 M V3 136M	0.87 to (0.96 to)	1.33) 1.49) C RTD 400MG C RTD 200MG	1.13 (0.92 1.22 (0.98 	to 1.40) to 1.52) M. NAPROMENT VS. 100MG BT 8.607	1.23 (0.5 NAPROXEN VS. D 200MS BID 3.247	NAPROXEN VS. 40PM. ET
	WEER 6: WEEK 12: OR TREATMONT 	MARY: : 4ACHA BID VX PEACBB.	CHIMA BID NY. PLANCEN	1.03 1.35 257 M V3 136M	0.87 to (0.96 to)	1.33) 1.49) C RTD 400MG C RTD 200MG	1.13 (0.92 1.22 (0.98 	to 1.40) to 1.52) M. NAPROMENT VS. 100MG BT 8.607	1.23 (0.5 NAPROXEN VS. D 200MS BID 3.247	NAPROXEN VS. 40PMS ET
	WEER 6: WEEK 12: OR TREATMONT 	MARY: 1 490MA BID 109 95ACBB. 	10 MA BID SE PLACES HOLDO C.000	1.03 1.35 1.35 1.06 1.06 1.06	1 0.87 to 10.96 to 10	1.33) 1.49) 1.870 400MG 2. VE 3.310 200MG	1.13 (8.92 1.22 (8.98 -SECONDARY ETD NAFROXE VE. BLD PLACER	E0 1.40) E0 1.52 EN NAPROXEN CO 186MG BT U.607 0.493	NAPROXEN VE. D 2004G BID 3.247 8.232	NAPROXEM VS. 400MG ET

- (a) This table is based on the last discretation carried forward approach
 (b) Scale range: from 0 to 6% with negative change indicating improvement
 (c) From Analysis of covariance model with treatment and center as factors and Easeline value as covariate,
 the corresponding nout MSE are: 11.005 for week 2, 12.177 for week 6, 12.555 for week 12
 (d) From a contrast statement from Analysis of Covariance model in (c), Agrican group was excluded
 (a) Q-EATTO 13 dolined as the table of least square mean changes from (c), of SC-58635 group versus haptened (f) From a contrast statement from Analysis of Covariance model in (c)

 * Statistically significant according to the Hochberg procedure(primary pairwise comparisons only)

BEST POSSIBLE

Table A.37.1 Number of Swollen Joints (Protocol 023)

TABLE 19 NUMBER OF SWOLLEN JOINTS
PART 1 OF 5: OBSERVED MEANS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO (K=221)	6C-58635 10CMG BID (N=228)	8C-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)
BASELINE			218	217	218
ĸ	221	228		20.5	20.6
MEAN	19.7	20.0	21.2	10.93	12.00
STD DEV	11.95	11.77	11.69	10.93	12.00
WKEK 2			218	217	218
Ħ	221	228		13.7	13.4
MEAH	16.0	13.7	13.6	9.18	10.22
STD DEV	12.73	10.78	11.19	9.10	10.22
MEER 6			***	217	218
¥	221	228	218	13.5	13.6
HELAN	15.8	13.0	14.2		11.32
STD DEV	13.43	10.87	12.21	9.59	11.32
WEER 12				212	218
N	221	228	216	217	13.9
REVA	16.0	13.9	14.4	13.6	
SID DEV	13.39	10.81	12.26	9.47	11.76

NUMBER OF SWOLLEN JOINTS PART 2 OF 5: PATIENT'S OVERALL STATUS IN CHANGE FROM BASELINE, NUMBER OF PATIENTS (%) (4)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO	SC-58635 100MG BID	SC-58635 200MG BID	8C-58635 400MG BID	NAPROXEN 500MG BID	LINEAR TREND
	(N=221)	(N=228)	(N=218)	(N=217)	(N=218)	p-VALUE (d)
						0.191
WEEK 2		72 (225)	89 (41%)	68(31%)	86(39%)	
IMPROVED (b)	66(30%)	72(32%)		142(65%)	127(58%)	
NO CHANGE	136(62%)	147(64%)	120(55%)		5(2%)	
WORSENED (c)	19(9%)	9 (4%)	9(4%)	7(3%)	3(24)	
	004/48083	228 (100%)	218(100%)	217 (100%)	218(100%)	
TOTAL	221(100%)	228(1004)	2.5(1004)	24. (2)		
						0.324
WEEK 6	81(37%)	76(33%)	90(41%)	76(35%)	93(43%)	
IMPROVED (b)			121(56%)	132(61%)	117(54%)	
NO CHANGE	117(53%)	144(63%)			8(4%)	
WORSENED (C)	23(10%)	B(4%)	7 (3%)	9(4%)	01, 6-7,	
TOTAL	221(100%)	228(100%)	218(100%)	217 (100%)	218(100%)	
10122						0.069
WEEK 12					03/ 43%1	*****
IMPROVED (b)	67 (30%)	73 (32%)	90(41%)	74(34%)	92(42%)	
	133(60%)	145(64%)	119(55%)	134(62%)	113(52%)	
NO CHANGE	21(10%)	10(4%)	9 ('4%)	9 (&%)	13(6%)	
WORSENED (c)						
	221(100%)	228(100%)	218 (100%)	217 (100%)	218(100%)	
WYPAT.	221,200-,					

D-VALUES FOR TREATMENT COMPARISONS (*)

	1 PRT	MARY1				SECO	MDARY			
				200MG BID Vs. 100MG BID	400MG BID VS.	400MG BID VS. 200MG BID	VØ.	VS.	VS.	VS.
TEEK 2:	0.003*	0.468	0.365	0.054	0.879	0.022 0.101	0.010	0.095	0.764	0.065 0.081
VEEK 6:	0.033	C.896 C.269	0.931	0.033	0.701	C.C83	0.007	0.074	0.669	0.148

⁽a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 66 with lower score as better
By definition, in this and subsequent afficacy tables, the ITT cohort includes only patients who had at least one dose of study medication

 ⁽a) This table is based on the last observation carried forward approach
 (b) Improved is defined as number of improved joints minus number of worsened joints is larger than or equal to 50% of the number of joints with baseline score > 0
 (c) Morsened is defined as number of worsened joints minus number of improved joints is larger than or equal to 50% of the number of joints with baseline score > 0
 (d) Cochran-Hantel-Raenszel test of linear dose trend stratified by center (Ronzero Correlation), Maproxen group was excluded
 (e) Cochran-Hantel-Haenszel test of treatment comparison stratified by center (Row Mean Scores Differ)
 Statistically significant according to the Mochberg procedure (primary pairwise comparisons only)

Table A.37.2 Number of Swollen Joints (Protocol 023)

NUMBER OF SMOLLEN JOINTS PART 3 OF 5: MEAN CHANGE ANALYSIS (a) (b) INTENT-TO-TREAT CONORT (ITT)

			PLACE		100	8635 G BID	200M	G BID	400	MG BID	NAPROXEN 500MG BID		LINEAR TREND
			(日=22	1)	(N=2	28)	(N=2	18)	(N•	217)	(N=218)	p-VALUE(c)	p-value(d)
												<0.001	<0.001
WEEK 2 OBSERVED M	PAN CHANCE		-1.	e	-6	. 3	-7	. 6		-6.8	-7.2		
STD DEV	EAR CHARGE		9.	_		.32				8.18			
LE MEAN CH	ANCE (c)			9		. 3	-7	. 1	-	-6.6	-6.8		
WEEK 6												0.003	0.001
OBSERVED M	PAN CHANGE		-3.	9	-6	. 2	-7	. 0		-6.9	-7.0		
STD DEV			10.	01	9	.46	9	. 42		8.98	8.99		
LS MEAN CH	ANGE (c)		-3.	8	- 5	. 9	-6	5.2		-6.4	-6.4		
WEEK 12												D.006	0.002
	EAN CHANGE		-3.	7	-6	. 0	-6	6. B		-6.9	-6.6		
STD DEV			10.	40	9	. 61	9	.70		9.67	10.05		
LS MEAN CH	LANGE (c)		-3.	7	-5	. 9	- 6	.0		-6.4	-6.1		
Q-RATIO WITH	95% CONFID	ENCE INTERV	ALS (e):	10000	BID	V8. NA	PROXES	1 :	200MG	BID VS. 1	NAPROXEN	400MG BID	vs. Kaproxei
	WEEK 2:			0.92	(0.	74 to	1.15)	,	1.04	(0.85 to	1.29)	0.96 (0.	77 to 1.20
	WEEK 6:		_								1.25)		77 to 1.29
	WEEK 12:			0.97	(0.	73 to	1.28)	•	0.99	(0.75 to	0 1.31)	1.04 (0.	79 to 1.37
p-VALUES FOR	TREATMENT	COMPARISONS	(f):										
	PRI	MARY							- 5500	MDARY			
	200MG BID	400MG BID	100MG BID	20036	BID	400MG	BID	4 0 0 MG	BID	NAPROXEN	NAPROXEN	MAPROXEN	MAPROXEM
	VS.		VS.	V		VS		V3	-	VS.		VS.	VB.
	PLACEBO		PLACEBO			100MG				PLACEBO	100MG BI		
WEEK 2:	- 0 0010	<0.001*	40 001	0.24		0.69	A	0.44	3	<0.001	0.453	0.681	0.721
WEEK 6:	0.002*	0.001*	0.006	0.7	25	0.56	3	0.82	2	<0.001	0.546	0.803	0.901
	0.004*	0.001*	0.006	0.8	66	0.58	12	0.70	6	0.003	0.819	0.952	0.751

⁽a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 66 with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and Baseline value as covariate,
the corresponding ROOT MSE are: 7.375 for week 2, 8.151 for week 6, 8.456 for week 12
(d) From a contrast statement from Analysis of Covariance model in (c), Naproxem group was excluded
(e) Q-RATIO is defined as the ratio of least square mean changes from (c), of SC-58635 group versus Naproxem group
(f) From a contrast statement from Analysis of Covariance model in (c)
* Statistically significant according to the Nochberg procedure(primary pairwise comparisons only)

Table A.38.1 ACR-20 Responder Index (Protocol 023-ITT)

9C-58635 COMPARATIVE EFFICACY AND BAFETY VS MAPROXEN IN RA M49-96-02-023

TABLE 16 CATEGORIAL STATUS BASED ON THE ACR RESPONDERS INDEX (20%) (a) MURGAER OF PATIENTS (%)

INTENT-TO-TREAT COMORT (ITT)

	PLACEBO	8C-58635	SC-58635	sc-58635	MAPROXEN	LIMEAR
	PLALEBO	100MG BID	200MG BID	400mg BID	500MG BID	TREND
	(N=221)	(M=220)	(N=218)	(M=217)	(N=218)	P-VALUE (c)
NEEK2					,	<0.001
INPROVED (b)	55 (25%)	95(42%)	101(46%)	93 (43%)	97(44%)	
NOT IMPROVED	166(75%)	133(58%)	117(54%)	124(57%)	121(56%)	
TOTAL	221(100%)	228(100%)	218(100%)	217 (100%)	218(100%)	
burner C						<0.001
MEEK6 (b)	60 (27%)	87(38%)	89(41%)	94(43%)	101(16%)	
NOT INPROVED	161(73%)	141(62%)	129(59%)	123(57%)	117(54%)	
TOTAL	221(100%)	228(100%)	218(100%)	217 (100%)	218(100%)	
WEEK12						<0.001
IMPROVED (b)	50(23%)	68 (3D%)	86(39%)	79 (36%)	91(42%)	
NOT INPROVED	171(77%)	160(70%)	132(61%)	138(64%)	127(58%)	
TOTAL	221 (100%)	228(100%)	218(100%)	217 (100%)	218(100%)	

P-VALUE FOR TREATMENT COMPARISONS (d):

	200MG BID VS. PLACEBO	MARY	,		400MG BID VS.	400MG BID VS.	NAPROXEN VS.	NAPROXEN VS. 100MG BID	VS. 200MG BID	VS. 400MG BID
WEEK2 1	<0.001*	<0.001*	<0.001	0.261	0.835	0.346	<0.001	0.537	0.698	0.507
WEEK6	0.002*	<0.001"	0.015	0.507	0.299	0.661	<0.001	0.096	0.294	0.507
WEEK12 :	<0.001*	0.002*	0.060	0.036	0.198	0.432	<0.001	0.011	0.585	0.242

Note: The ITT cohort includes only patients who had at least one dose of study medication

(a) This table is based on the last observation carried forward approach

(b) Improved: At least 20% improvement from baseline in the number of tendar/peinful joints and in the number of swollen joints as well as at least 20% improvement from baseline in at least three of the following assessments:

1) Physician's Global 2) Patient's Global 3) Patient's Assessment of Pain 4) C-Reactive Protein 5) HAQ Functional Disability Index

(c) Contrangulation of the
Index
(c) Cochran-Mantel-Haenszel test of linear dose trend stratified by center, p-value for Honzero Correlation, naproxen was excluded
(d) Cochran-Mantel-Haenszel test of treatment comparison stratified by center, p-value for Row Mean Scores Differ
* Statistically significant according to the Mochberg procedure(primary pairwise comparisons only)

Table A.38.2 ACR-20 Responder Index (Protocol 022, ITT)

solfield comparative efficacy and usi safety vs naproxen in RA $_{\rm N45-96+02}$ dis

TABLE 18 CAREGIBICAL STATUS EASED ON THE ACK RESPONDERS INDEX (20%) (A) ICHMEEN OF PATIENTS (*)

INTEND 10 TREAT COMOST (101)

	FUACEBO	35° - 7° - 6° 5°	87-586-5	SC-18tin	MARSAKEN	LINEAR
	124 [[3.6]	icomo sis Silaco	200MS BID (N. 235)	402M3 DID 31:7:7:	FA CIR: EAGNO PID	TT END C MALUE (41)
::::::::::::::::::::::::::::::::::::::						e. 1981
1899.020 00	514 25%)	997 40%	115: 19%:	394 41% 1	899 46 NO	
COT THEF PIED	1875 78%	145 (779)	1000 F1M3	12%: 59%;	[563 B56]	
194AL	231+267€0	145 (100%)	2051100%)	117 (16 3%)	12.3260%	
WEEK					•	eu. 361
(A) CENTROVED	ଞ୍ଜ(20€)	93 (39 k)	114 (49%)	877 45 4 7	84 (37 €)	
NOT IMPROVED	167(72%)	147(-61%)	121(524)	130: 60 k)	141: 63%)	
TOTAL	291(100%)	240(100%)	235 (100%)	217 (100€)	225(100%)	
WEEK12						0.005
IMPROVED (b)	65(29%)	95 (45%)	103 (44%)	a5(39%)	#1(36%)	
NOT IMPROVED	195 (71%)	145(50%)	132 (56%)	132(61%)	144(64%)	
TOTAL	231 (200%)	240 (100%)	235(100%)	217(100%)	225 (100%)	

P-VALUE FOR TREATMENT COMPARTSONS (d):

	- PS1	MARY			SECURDASY							
	200MO BIT VS. PLACEBO	400M9 BID VS. PLACEBO	VS.	V\$.	VS.	us.	vs.		vs.	NAPAGREDI VA. 400MG EID		
WEEKS : WEEKS :	<0.001.	<0.000* 0.605* 0.012*	40.303 0.008 0.005	0.060 0.000 0.000	5.586 5.693 0.956	0,160 0,047 0,320	<0.001 0.002 0.049	0.848 0.817 0.445	0.028 9.61 0.676	C.561 C.578 C.562		

BEST POSSIBLE

⁽a) This table is based on the last observation carried forward approach
(b) improved: At least 20% improvement from baseline in the number of tender(painful joints and in the number of
(a) Iten joints as well as at least 20% improvement from baseline in at least three of the following assessments:
(i) Physiciants Giolad 2) Patient's Global 3) Patient's Assessment of Pain 4) C-Rosotive Protoin 5) HAG Functional Lisability
(a) OcchrantMantsi-Ha-mapel test of linear dies tiend stratified by center, preduce for Bonzero Correlation, naprowen was excluded
(a) CochrantMantsi-Ha-mapel test of flustrost objection stratified by center, preduce for Bonzero Correlation, naprowen was excluded
(a) CochrantMantsi-Ha-mapel test of flustrost objection stratified by center, preduce for Bonzero Correlation of the Statistically significant according to the Birthery pairwise comparisons only)

Table A.38.3 ACR-20 Responder Index (Protocol 023-Evaluable)

EC-11415 CUMPAGALINY EFFICACY AND SAFETY VS NAWXONEN IN RA 200 96 00 027

APPENDIX 5.2.. CATEGORIAL STATES EASED ON THE ARK RESPONDERS INDEX (20%) (NRBER OF PATIENTS (%)

WZEF 2 : WFRK 6 : WEEK 12:	0.018 0.611 0.442	0.021 0.589 0.139	0.018 0.103 0.229	0.969 0.910 0.633	0.850 0.139 0.069	0.906 0.155 0.528	<0.001 0.046 0.029	0.338 0.093 0.014	0.273 0.265 0.980	0.354 0.730 0.664
	100MG BID VS. MLAGEBG	206MS BID VS. PEACEBU	UTOMO PID ME. PLACEBO	VS.	400MG BID VR. 100MG BID	400MG BID VS. 200MG BID	VS.	NAPROXEN VS. 100MG B1D	NARFOXEN VS. 200MJ BID	NAPPONEN VS. 130Mo BLD
P-VALUE TOP TETA	ATMENT COMEA	CIBYS 1112								
IMPERVÕD IA. NUT IMPROVED ITAL		## + (4) 06(-57+) #2(210%)	1.7.	6 91 17:81	1141 36 187110	1:1	97(52%) 1867(59%)	9	81 519 911634	
F DWLL					93: <u>4</u> 4		S9 (49%)		11 434	7.401
IMPROVED (A) DOT IMPROVED TOTAL		27 (46 8) 30 (54%) 59 (1008)	237	5181	38 (27 162 (12)	¥*	43; 43%) 108(100%)	4	1: 37%; 0::01:01:	
WEEK IX		*******	10.	4031	€ 4 1 63		65(60 k)	6	13 (62%)	0.002
IMPROVED (a) NOT IMPROVED TOTAL		397 51%) 367 49%) 74(130%)	55	1491 1491 1491	68 (52 64 (46 132 (199	£.	78: 61%) 30: 39%) 128:(100%)	5	51 60%) 61 40%) 1(100%)	
WEER 6										0.080
IMWEDVED (A) NOT IMPROVED TOTAL		40+ 36%) 95+ 46%; 36;320+3	94.	4561 5491 10091	941 47 941 53 1781100	% ;	82(47%) 93(59%) 135(130%)	ë	21 51%: 71 4983 91160%:	
WINE 4										1.114
		1ACEBO 11 221)*	80 - J 1966 61 - 1	4 E1D	\$0-5863 100MG B (\$1219)	10	80-58035 460M3 E16 (N.017)*	5.3	PROXEN GMG BIT - 216)*	TIMEAR TRANSCORE

⁽a) improved: At least 20% improvement from baseline in the number of tender/painful joints and in the number of swollen joints as well as at least 20% approvement from baseline in at least three of the following assessment:

1) Physician's Global 2: Patient's Global 3: Patient's Assessment of Pain 4: C-Reactive Protein 5: MAC Tunctional Disability

BEST POSSIBLE

index.

Cochran Montel Hasnszel test of linear dose trans stratified by center, p-value for Nonzero Correlation, maproxen was excluded to: Cochran-Mantel-Hasnszel (est of treatment corperison stratified by center, p-value for Now Mean Scores Differ > All hardenized patients

Table A.39.1 ACR-50 Responder Index (Protocol 022-ITT)

GC-55% IS COMPARATIVE ETTICACY AND US: CAMETY VS NAFROXEN IN RAIN 16 96 II 912

TABLE 31

GAGERHIGH STATUS HARRO IN THE ALK BESPONUES (MICEX (55%) (G)

SUMMER OF PATIENTS (%)

INTEND OF THEAT SCHOOL (1979)

	a enancit	E17 - 5 - 6 - 5 -	SC+56115 403M3 BID	NAPROXEN 500MG MED	LINEAR TREND
34 (2, 1)	1.1M3 111 3. 447	211 3 3 E15 46 215.	.N-2104	(x 225)	F VALUE (c)
					<0.001
14 - 441	22.1 (25)	2.1 (25%)	34: 15%;	28 (12%)	
237: 94*)	118° 91 4 .	1001 65%:	1631 6481	197(88%)	
233 (2014)	140/100%;	235(100%)	217:100%)	225 (100%)	
					<0.001
157 843	29 (124)	401 178)	30(171)	29 (134)	
213(92%)	211 (88%)	195 (B3%)	181(93%)	196(87%)	
131(100#)	248(188*)	235:100%;	117(100%)	225(1004)	
					.0.001
\$ 4.4 · · · ·	ia ti∀.	40 (0.29)	36(174)	29 (13 %)	
214, 91*.	2.44 F #14 %	:941 63%)	181(83%)	196(87%)	
231717181	24 % 5 Kd • 1	2.65 (1628)	512(100*)	R25(100%)	
	14: (4) 21% 949 233(1604) 16(88) 213, 924) 131(1604)	14 14 14 14 14 15 14 15 14 15 15	10 2.11	13	10

P'ONTARE ROR TERROMERT OF MENAGERS IN F

•	WA.	26.	Value	5,4.	18.	DECMO PID	VE. PLACEBO	VS. TORMO ATD	WS,	
WEEK! WEEK!	2.361	3.519	1 104	1	2.14	6,649 6,670	5.841	0.161 0.602	0.197	1.224

BEST POSSIBLE

This facing it besond to the less office court of forward appropriate painful joints and in the number of the largevers at season los opprovement for resemble in the number of tender painful joints and in the number of the less than joints as well as at least 50% improvement from baseline in at least three of the following assessments:

10 Expanding Joint 17 Patient's Slobs. 33 Entient's Assessment of Pain 40 Scheedive Protein 50 HAC Functional Disability Lines.

10. Porhram Manual Baenszel test of linear fore trend stratified by center, p value for Bonzefo Correlation, maprovem was excluded the Orderon Manual Baenszel test of trealogist Comparison stratified by center, p-value for Row Mean Scores Differ

Table A.39.2 ACR-50 Responder Index (Protocol 023-ITT)

SO-58635 COMPARATIVE EFFICACY AND SAFETY US NAPROXED IN PA NG9 90 02 123

TABLE 19 CATEGORIAL STATUS EFFEL OF THE AUF FESTIMBERS INDEX (200) (a) NUMBER OF PACIESTS \mathcal{A}^{\bullet}

INTEND TO TELA. CUBUST SIVIL

	P(AdEBC (2. 121)	90-58435 100MO BID (N.228)	955-448-35 20089-215 181-2161	90-56635 569M2 EID 68-223)	NAPRONEM BOOMS BID (N. 218)	LIMFAR TREND F VALUE OCT
						0.000
MEEKI MEEKI	12(34)	241 (18)	37: 17%;	27 (12%)	234 (234)	
BUT IMPROVED	2031 4583	202(99%)	1811 87*1	190(88%)	185(05%)	
TOTAL	1111105%	228:10CN:	218(130*)	237 (240%)	1187100%1	
11.11.00						
эдрке						0.008
IMPROVNE (b)	154 717	22€ 10%:	35(16%)	251 124)	32(15%)	
NOT IMPROVED	206: 93%)	2061 90%)	135(84%)	192(86%)	186(85%)	
TOTAL	201(109%)	228(100%)	218(100%)	217(200%)	SIE(200#)	
						9,200
WEEKIZ		73 (IC%)	38: 17*)	27 (10%)	39(19%)	
IMPROVED (b)	33(6%)	2051 90%)	1801 93%)	190(68%)	179 (86%)	
NOT IMPROVED	308(94%)	2071 9061	**************************************	*****		
moves (231 (100%)	276 (100%)	218:11:01:	219(130%)	218(100%)	
TOTAL	A	A				

P-UALGE FOR TREATMENT COMPARTSONS (d):

	200MG B10 V8. PLACEBO	400MG BID VS. PLACEBO	VS.	VS.	469MG 61D VS. 100MG RTD	VS.	₹₹,	NAPROXEN VS. 100MC BID	NAPROXEN US. PERMO RID	RAPROXÉR VS. 400MG RID
WEEKO	49.861	3.010	6.019	6.115	0.795	0.142	<0.901	0.275	0.820	6.324
WEEKO:	0.861	0.664	6.245	6.640	0.587	0.147	0.906		0.72.	0.132
WEEKO2::	40.601	9.017	0.061	6.630	0.519	0.112	<0.901		0.810	0.323

- Note: The III domnit includes only patients who had at least one died of study medication

 [a) This table is based on the last observation carried forward approach

 [b) improved: At least 10% improvement from baseline in the number of tender/painful joints and in the number of

 sw. Fig. Formation as well as at least 50% improvement from baseline in at least three of the following assessments:

 [b) Private Introduction (Local 2) Particular Coral () Patronic Admissions of Path 4) C-Reactive Protein b) HAV Punctional Disability

 index

 [c) Obstrain-Manuel-Hamissel test of Linear disw trend stratified by renter, p-value for Nonzelo Correlation, daptoxed was excluded

 [d) Occupan-Manuel-Hamissel test of Index of realized companies stratified by conter, p-value to: Now Mean Secret Differ

BEST POSSIBLE

Table A.40 Patient's Assessment of Arthritis Pain-VAS (Protocol 023)

SC-58635 COMPARATIVE EFFICACY AND SAFETY VE NAPROXEN IN RA H49-96-02-023

TABLE 21 PATIENT'S ASSESSMENT OF ARTHRITIS PAIN (VAS) PART 1 OF 3: OBSERVED MEANS (a) (b)

INTENT-TO-TREAT COMORT (ITT)

	PLACEBO (N=221)	SC-58635 100MG BID (N+228)	SC-58635 200MG BID (N=218)	6C-58635 400MG BID (N=217)	MAPROXEN 500MG BID (N=218)
BASELINE			310	216	218
N	220	228	218	67.B	66.8
KRAH	68.1	66.1	67.9		18.48
STD DEV	19.57	20.13	19.90	19.70	10.40
WEEK 2					
N	220	228	218	217	218
MEAN	58.7	45.8	41.4	42.2	40.6
STD DEV	27.15	26.25	25.10	24.62	24.36
WEEK 6					
N.	221	228	218	217	218
mean Mean	60.5	47.8	46.5	45.6	43.7
STD DEV	27.86	27.74	28.38	26.39	25.77
WREK 12					
N	221	228	218	217	218
KEAN	62.0	51.0	47.0	48.7	44.6
			29.03	26.48	27.43
STD DEV	27.88	28.41	29.03	26.48	21.4.

(a) This table is based on the last observation carried forward approach
(b) Scale ranged from 0 to 100 mm with lower score as better
* By definition, in this and subsequent efficacy tables, the ITT cohort includes only patients who had at least

one dose of study medication

PATIENT'S ASSESSMENT OF ARTHRITIS PAIN (VAS) PART 2 OF 3: MEAN CHANGE ANALYSIS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO {N=221}	100MG BID	8C-58635 200MG BID (N=218)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)	OVERALL p-value(c)	LINEAR TREND D-VALUE(d)
						<0.001	<0.001
WEER 2	-9.4	-20.3	-26.5	-25.6	-26.2		
OBSERVED MEAN CHANGE	-		24.12	23.61	25.02		
STD DEV	25.81	-20.7	-26.0	-25.1	-26.1		
LS MEAN CHANGE (c)	-8.8	-20.7	-20.0				
						<0.001	<0.001
MEEK 6	-7.4	-18.3	-21.4	-22.2	-23.1		
OBSERVED MEAN CHANGE	25.59		28.80	27.60	26.35		
STD DEV		-18.3	-20.4	-21.1	-22.5		
LS MEAN CHANCE (c)	-6.1	-18.3	-20.4	-41.1			
						<0.001	<0.001
WEEK 12		-15-1	-20.9	-19.0	-22.1		
OBSERVED MEAN CHANGE	-6.1		29.12	27.10	27.77		
STD DEV	25.01			-18.5	-22.0		
LS MEAN CHANGE (c)	-5.5	-15.5	-20.4	-18.5	-22.0		
Q-RATIO WITH 95% CONFIDENC	CE INTERVALS (a):	100mg BID VS. N	APROXIEN	200MG BID Vs.	NAPROXEN	400MG BID	vs. Maproxen
		0.79 (0.65 to	0.961	1.00 (0.84	to 1.18)	0.96 (0.	80 to 1.14)
	EEK 2:	0.81 (0.63 to		0.90 (0.72			75 to 1.17)
	EEK 6:			0.93 (0.73			65 to 1.07)
WZ	EEK 13:	0.71 (0.53 to	0.52;	0.33 (0.73	2110)		,

p-values for treatment comparisons (f):

	100MG BID VS. PLACEBO	200MG BID VS. PLACESO	400MG BID VS. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	400MG BID V8. 200MG BID	VS.	NAPROXEN V8. 100MG BID	WAPROXEM VS. 200MG BID	VS. 400MG BID
WEEK 2:	<0.001	<0.001	<0.001	0.014	0.046	0.655	<0.001	0.012	0.962	0.620
WEEK 6:	<0.001	<0.001	<0.001	0.380	0.233	0.753	<0.001	0.073	0.364	0.555
WEEK 12:	<0.001	<0.001	<0.001	0.042	0.226	0.419	<0.001	0.007	0.519	0.146

 ⁽a) This table is based on the last observation carried forward approach
 (b) Scale ranged from 0 to 100 (sm) with negative change indicating improvement
 (c) From Analysis of Covariance model with treatment and center as factors and baseline value as covariate, the corresponding ROOT MSE are: 22.76 for week 2, 24.88 for week 6, and 25.35 for week 12
 (d) From a contrast statement from analysis of Covariance model in (c), Naproxem group was excluded
 (e) Q-RATIO is defined as the ratio of least square mean changes from (c), of SC-58635 group versus Naproxem group
 (f) From a contrast statement from Analysis of Covariance model in (c)

Table A.41 C-Reactive Protein (Protocol 023)

9C-58635 COMPARATIVE EFFICACY AND SAFETY VS NAPROXEN IN RA 849-96-02-023

C-REACTIVE PROTEIN PART 1 OF 2: OBSERVED HEARS (a) (b)

INTERT-TO-TREAT COHORT (III)

		1011221 10 11221			
	PLACEBO (N=221)	SC-58635 100MG BID (N=228)	SC-58635 200MG BID (N=210)	SC-58635 400MG BID (N=217)	NAPROXEN 500MG BID (N=218)
BASELIME S MEAN STD DEV	215 15572.1 15608.32	222 16464.0 19890.11	214 17887-9 20419.69	210 15590.5 15790.92	210 15481.0 18677.37
WEEK 2 M MEAN STD DEV	220 15154.5 16015.79	228 16592.1 20979.44	218 17367.0 20191.55	216 16935.2 17566.50	217 14023.0 14229.42
Week 6 M Mean Std Dev	221 16470.6 18308.60	228 17693.0 22025.47	218 17243.1 19269.39	217 18638.7 20799.01	218 14504.6 15386.34
WEEK 12 H HEAN STD DEV	221 18040.7 27587.43	228 16877.2 20610.35	218 16825.7 18969.70	217 17963.1 19711.54	218 13756.9 13783.06

⁽a) This table is based on the last observation carried forward approach

C-REACTIVE PROTEIN PART 2 OF 2: MEAN CHANGE ANALYSIS (a) (b)

INTENT-TO-TREAT COHORT (ITT)

	PLACEBO	8C-58635 100MG BID	SC-58635 200MG BID	8C~58635 400MG BID	MAPROXEN 500MG BID	OVERALL	LINEAR TREND
	(N=221)	(N=228)	(N=218)	(N=217)	(N=218)	p-VALUE(c)	D-AYTHE (q)
						0.168	0.159
WEEK 2	-325.6	333.3	-359.8	1409.5	-1352.4		
OBSERVED REAN CHANGE	12853.82	11978.74	15069.37	12330.92	12025.87		
STD DEV		703.6	374.8	1535.4	-1247.1		
LE MEAN CHANGE (c)	-300.7	743.0	374.0	2333.0			
						0.016	0.172
MEEK 6		1260 4	-542.1	3347.6	-823.8		
OBSERVED MEAN CHANGE	1004.7	1369.4		15726.68	13705.46		
STD DEV	15781.95	13404.89	12134.44		-340.8		
LE MEAN CHANGE (c)	1420.0	2106.5	395.5	3871.3	-340.0		
						0.040	0.912
WEEK 12	2624 7	536.0	-967.3	2595.2	-1600.0		
OBSERVED MEAN CHANGE	2604.7			16625.43	12311.82		
STD DEV	26246.44	14431.49	14446.40		-1269.8		
LS NEAM CHANGE (c)	2778.4	1236.1	37.6	2990.0	-1403.6		
Q-RATIO WITE 95% CONFIDENCE INTERVALS	(e): 100#	es BID VS. NA	PROXEE	200MG BID VS.	HAPROXEN	400MG BID	vs. Naprozen

-0.56 (BOH-ESTIMABLE) -6.18 (BOH-ESTIMABLE) -0.97 (BOH-ESTIMABLE) -0.30 (BON-ESTIMABLE) WEEK 2: -11.4 (MON-ESTIMABLE) -2.35 (MON-ESTIMABLE) -1.16 (NON-ESTIMABLE) -0.03 (NON-ESTIMABLE) WEEK 6: WEEK 12:

p-values for treatment comparisons (f):

	100MG BID VS. PLACEBO	200MG BID VS. PLACEBO	400MG BID VS. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	400MG BID VS. 200MG BID	VS.	WAPROXEN VS. 100MG BID	VS. 200MG BID	WAPROXEN VS. 400MG BID
WEEK 2: WEEK 6:	0.383 0.595	0.561 0.432	0.115 0.061 0.896	0.775 C.186 0.452	0.472 0.175 0.273	0.320 0.008 0.068	0.417 0.179 0.012	0.091 0.060 0.117	0.164 0.574 0.418	0.018 0.001 0.009

 ⁽b) Unit of measurement : ug/L
 By definition, in this and subsequent efficacy tables, the ITT cohort includes only patients who had at least one dose of study medication

⁽a) This table is based on the last observation carried forward approach
(b) Unit of measurement r ug/L with negative change indicating improvement
(c) From Analysis of Covariance model with treatment and center as factors and baseline value as covariate,
the corresponding ROOT MSE are: 1963 for week 2, 13440 for week 6, and 16562 for week 12
(d) From a contrast statement from analysis of Covariance model in (c), Maproxem group was excluded
(e) Q-RATIO is defined as the ratio of least square mean changes from (c), of 82-58635 group varsus Naproxem group
(f) From a contrast statement from Analysis of Covariance model in (c)

Table A.42 HAQ Functional Disability Index (Protocol 023)

SC-58635 COMPARATIVE EFFICACY AND SAFETY VS NAPROXEN IN RA E49-96-02-023

TABLE 25 HAQ FUNCTIONAL DISABILITY INDEX PART 1 OF 3: OBSERVED HEARS (4) (b)

	PLACEBO (N=221)	SC-58635 100MG BID (M=228)	8C-58635 200MG BID (N=218)	8C-58635 400MG BID (Me217)	MAPROXEN 500MG BID (N=218)
BASELINE					
M	219	226	217	216	218
MEAN	1.4	1.4	1.3	1.3	1.4
STD DEV	0.68	0.70	0.67	0.63	0.68
WEBK 2					
N	221	228	218	217	218
MEAN	1.3	1.1	1.0	1.0	1.1
STD DEV	0.67	0.69	0.68	0.64	0.67
WEEK 6					
¥	221	228	216	217	218
MEAN	1.3	1.2	1.1	1.0	1.1
STO DEV	0.72	0.71	0.72	0.66	0.69
WEICK 12					
¥	221	228	218	217	218
MEAN	1.3	1.3	1.1	1.1	1.1
STD DEV	0.73	0.70	0.73	0.67	0.68

⁽a) This table is based on the last observation carried forward approach

MAQ FUNCTIONAL DISABILITY INDEX PART 2 OF 3: HEAN CHANGE AMALYSIS (a) (b)

INTENT-TO-TREAT CONORT (ITT)

	PLACEBO	SC-58635 100MG BID	SC-58635 200MG BID	8C-58635 400MG BID	NAPROXEN 500MG BID	OVERALL	LINEAR TREED
	(N=221)	(N=228)	(N=218)	(N=217)	(N=218)	p-VALUE(c)	D-ATTRE(q)
WEEK 2						<0.001	<0.001
ORSERVED MEAN CHANGE	-0.1	-0.2	-0.3	-0.3	-0.3		
STD DEV	0.44	0.42	0.45	0.47	0.47		
LS MEAN CHANGE (c)	-0.1	-0.2	-0.3	-0.3	-0.3		
WEEK 6						<0.001	<0.001
OBSERVED MEAN CHANGE	-0.1	-0.2	-0.3	-0.3	-0.3		
STD DEV	0.49	0.43	0.51	0.52	0.48		
LO NEAM CHANGE (c)	-0.1	-0.2	-0.3	-0.3	-0.3		
WEER 12						<0.001	<0.001
OBSERVED MEAN CRANGE	-0.1	-0.1	-0.2	-0.2	-0.3		
STD DEV	0.49	0.44	0.51	0.53	0.48		
LS NEAM CHANGE (c)	-0.1	-0.1	-0.2	-0.2	-0.3		
Q-RATIO WITH 95% CONFIDENCE INTERVA	LS (e): 1901	40 BID VS. MA	PROXIEN	200MG BID VS.	NAPROXEN	400MG BID	vs. Naproxem
WEEZEK 2:	0.:	3 (0.59 to	1.15)	1.08 (0.82	to 1.45)	1.05 (0.	79 to 1.42)
WEEK 61	0.	69 (0.43 to	1.04)	1.07 (0.76	to 1.51)	0.99 (0.	69 to 1.41)
WEEK 12:	0.	56 (0.30 to	0.90)	0.94 (0.64	to 1.38)	0.98 (0.	67 to 1.43)

p-VALUES FOR TREATMENT COMPARISONS (f):

	100MG BID VS. PLACEBO	200MG BID VS. PLACEBO	400MG BID V5. PLACEBO	200MG BID VS. 100MG BID	400MG BID VS. 100MG BID	VS.	Naproxen Vs. Placebo	NAPROXEN VS. 100MG BID	NAPROXEN VS. 200MG BID	NAPROXEN VS. 400MG BID
WIEDER 2:	<0.001	<0.001	<0.001	0.080	0.124	0.837	<0.001	0.244	0.560	0.707
WEEK 6:	0.006	<0.001	<0.001	0.025	0.074	0.658	<0.001	0.065	0.698	0.956
WEEK 12:	0.103	<0.001	<0.001	0.031	0.017	0.813	<0.001	0.012	0.738	0.923

⁽a) This table is based on the last observation carried forward approach

 ⁽a) Into table to based on the tast cover as less disability
 By definition, in this and subsequent efficacy tables, the ITT cohort includes only patients who had at least one dose of study medication

⁽a) This table is based on the last observation carried toward approximate.

(b) Scale ranged from 0 to 3 with negative change indicating improvement.

(c) From Analysis of Covariance model with treatment and center as factors and baseline value as covariate, the corresponding ROOT MSE are: 0.424 for week 2, 0.458 for week 6, and 0.462 for week 12.

(d) From a contrast statement from analysis of Covariance model in (c), Maproxam group was excluded.

(e) Q-RATIO is defined as the ratio of least square mean changes from (c), of BC-58615 group versus Maproxem group.

(f) From a contrast statement from Analysis of Covariance model in (c).

Table A.43 Withdrawal-Lack of Arthritis Efficacy (Protocols 022, 023)

Text Table 40. Reasons for Study Termination (All Randomized Patients: 12-Week Pivotal Studies 022 and 023 and 12-Week Pooled Pivotal Studies)

Studies)								
	Number of Rheumatoid Arthritis Patients by Treatment Group							
			Celecoxib		Naproxen			
Study	Placebo	100 mg BID	200 mg BID	400 mg BID	500 mg BID			
Study 022	(n=231)	(n=240)	(n=235)	(n=218)*	· (n=225)			
Total Completed	101 (44%)	154 (64%)	158 (67%)	137 (63%)	138 (61%)			
Total Withdrawn	130 (56%)	86 (36%)	77 (33%)	81 (37%)	87 (39%)			
Lost to Follow-up	3 (1%)	1 (<1%)	3 (1%)	1 (<1%)	1 (<1%)			
Pre-Existing Violation	2 (<1%)	1 (<1%)	3 (1%)	2 (<1%)	0 (0%)			
Protocol Non-Compliance	10 (4%)	4 (2%)	4 (2%)	7 (3%)	9 (4%)			
Treatment Failure	104 (45%)	67 (28%)	50 (21%)	59 (27%)	65 (29%)			
Adverse Event	11 (5%)	13 (5%)	17 (7%)	12 (6%)	12 (5%)			
Study 023	(n=221)	(n=228)	(n=219)*	(n=217)	(n=218)			
Total Completed	78(35%)	117 (51%)	124 (57%)	126 (58%)	133(61%)			
Total Withdrawn	143 (65%)	111 (49%)	95 (43%)	91 (42%)	85(39%)			
Lost to Follow-up	0 (0%)	0 (0%)	0 (0%)	2 (<1%)	0 (0%)			
Pre-Existing Violation	2(<1%)	2 (<1%)	3 (1%)	2 (<1%)	0 (0%)			
Protocol Non-Compliance	4 (2%)	5 (2%)	2 (<1%)	2 (<1%)	0 (0%)			
Treatment Failure	125 (57%)	92 (40%)	74 (34%)	69 (32%)	69(32%)			
Adverse Event	12 (5%)	12 (5%)	16 (7%)	16 (7%)	16 (7%)			
Pooled ^b	(n=452)	(n=468)	(n=454)*	(n=435) °	(n=443)			
Total Completed	179 (40%)	271 (58%)	282 (62%)	263 (60%)	271 (61%)			
Total Withdrawn	273 (60%)	197 (42%)	172 (38%)	172 (40%)	172 (39%)			
Lost to Follow-up	3 (<1%)	1 (<1%)	3 (<1%)	3 (<1%)	1 (<1%)			
Pre-Existing Violation	4 (<1%)	3 (<1%)	6 (1%)	4 (<1%)	0 (0%)			
Protocol Non-Compliance	14 (3%)	9 (2%)	6 (1%)	9 (2%)	9 (2%)			
Treatment Failure	229 (51%)	159(34%)	124 (27%)	128 (29%)	134 (30%)			
Adverse Event	23 (5%)	25 (5%)	33 (7%)	28 (6%)	28 (6%)			

Derived from Individual Study Reports

a) Total number of patients includes two patients (one in the celecoxib 200 mg BID group [Study 023] and one in the celecoxib 400 mg BID group [Study 022]) who were randomized but did not receive study medication and are not included in the ITT Cohort.

b) Pooled represents data from combined pivotal Studies 022 and 023.

Table A.44 Time to Withdrawal - Lack of Arthritis Efficacy (023)

BC-2006 COmparative inversor and baptet we mapped in has been comparative in the 10^{-10}

TABLE 20
TODA TO WITHDRAWNL DUE TO LACK OF ARTHURIS EPPCRAFT
PART 1 OF 2 MAYLAN—MINE REPRESENTS OF PROPRIENTS OF PARTIES THE ROLL HOUR REPRESENT THE TO LACK OF ARTHURIS SEPECAÇE

CHYBRY-70-TERMY COMMER (ITT)

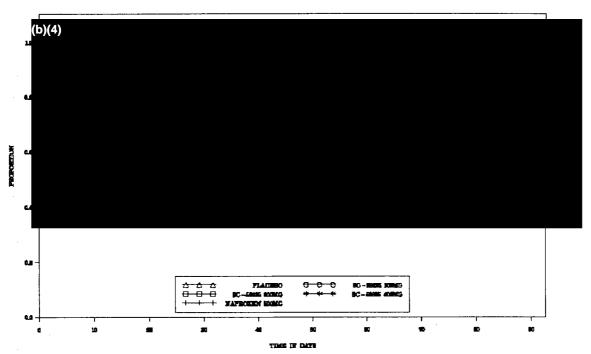


TABLE 28
TIME TO WITHDRAWAL DUE TO LACK OF ARTURITIS EFFICACY
FART 2 OF 2: LOG-RAWK TESTS FOR TIME TO WITHDRAWAL DUE TO LACK OF ARTERITIS EFFICACY

INTENT-TO-TREAT COMORT (ITT)

p-values for overall companisons (a):

<0.001

p-VALUES FOR TREATMENT COMPARISONS (b):

160MG BID	200mg BID	400MG BID	20000 BID	400ms BID	400MG BID	HAPROXXX	Maproxes	MAPROXEN	Kaproxen
VS.	YB.	٧ø.	VS.	VS.	YS.	V#.	V#.	Yø.	V#.
PLACEBO	PLACERO	PLACESO	100mg BID	100MG BID	250MG BID	PLACEBO	TOOMS BID	ZOOMS BID	400MG BID
					• • • • • • • •				
<0.001	<0.001	<0.001	0.092	0.046	0.774	<0.001	0.035	0.647	0.878

⁽a) From log-rank test for all five treatment groups (b) From pairwise log-rank test

Table A.45 Summary of Dosage change-OA /RA(protocol 024)

!Celecizir ISE FINAL dosecho PAGE 1 twole 9.7. Summary of Disage Changer Long Term Open Label Trial 024 Starting Dase Celectrib 100 mg BIS NO SHANGES 1931 19 34. 4691 14 74. 663 (-05.9%) 4441 67,441 4711 00,541 31 00,54 21 00,241 1375(71.3%) 1389(72.2%) 374 (33%) 1014(71.0%) 1006(20.7%) 4(0.2%) 2(< 0.1%) 2(< 0.2%) INCREASE IN DODE 100-200 100-300 100-400 OTHER 22: 2:78
10: 2:74
4: 0:0%
10: 0:0%
11: 0:2%
11: 0:2%
11: 0:2%
11: 0:0%
11: 0:2%
11: 0:0%
11: 0:0% 564 2.045 264 1.445 231 1.345 64 0.145 24 0.145 24 0.145 24 0.145 25 0.065 154 0.145 24 0.145 25 0.145 70; 3:18; 79; 1.5%; 79; 1.0%; 7; 0.1%; 7; 0.1%; 7; 0.1%; 2; 0.1%; 2; 0.1%; 7; 0.1%; 7; 0.1%; 7; 0.1%; 7; 0.1%; 7; 0.1%; 7; 0.1%;

Tipher' beans relectivit doses of 700 mg AM/200 mg PM, 200 mg AM/200 mg FM, 400 mg PM, 4

10% Backing 105

106 other 206

FIMAL

030UN98 08:20

Sureary of Posage Change: long Term Open Label Trial

			F	A		v w
Start Dope	Withdr	awals	Stil	l Active	Comb	rined
	(N =	523)	(1) =	: 1422)	(3) ≈	: 1945)
Lecoxib 200 mg BIB						
NO CHANGES	131; 23),[%]	315 (22.2%)	436 (22.4%)
INCREASE IN DOSE	3681 70	3.4%)	1023(71.9%) 26.3%) 45.6%)	1391(71.5%)
007 - 3 0 6	1274 00	.4%1	3744	26.3%)	491(25.2*)
266-400	151(40	ર,⊍\$ા	648(45.6%)	B99 (46.24)
OTHER	2 / 3	5.5 % (1 (<	0.1%)	1(<	(0.1%)
DECREASE IN DOSE	4 '	3.9 % 1	50	0.4%)	9 (0.5%)
MULTIPLE CHANGES				5.6%)		
200-100-300				0.3%)		
2785 = 176 = 21 H = 1 E 0	1:	7. 2 9 i	€ (0.0%)	3 (<	(0.1%)
208-200-200-200	2 '	1.081	1(-	< 0.1%) < 0.1%) O.0%)	2 (<	(0.1%)
200 100 201 300 400	_ : .	2 483	1(-	< 0.1₹)	3 (C.2%)
200-100-200-400	7 1	791	G (0.08)	3 (*	< 0.1%)
DP3+190+199+439+205				는, 3%)		
136 .10 440 109				0.0%)		
1 at day + 11 + +2 t2 +1 15		210	1 (-	6 (0.1%)	1.0	0.000
Supplied to the service of the first service of the		ari 💵 i	1 (-	< 0.1%) < 0.1%)	1 (-	< 0.1%)
	7.	3 (14)	1(-	< 0.1%)	2 (*	c 0,1%)
du li e a ae milita c				1.3%)		
16 3 ac-21 say				0.4%)		
15%=330+213+330+201	9:	0,081	2 (0.1%)	2(8.1%)
900 300 201 300 400	- 0	ଅ, ଅଶା	3 (0.2%) < 0.1%) 0.0%)	3.0	9 28)
1 - (4) (4) - (4) - 4 (1) - 4 (1) 4 (1) - 10 (2)		0.0%1	13-	< 0.1%)	3.5-	< 0.1(1)
200 300 430 100 Def (00 -400-100-600 1 0-306-400-4 0-300-400 200 306 400 -200-400 200-400640 -200-600 000-100-0000+200-300	2	C 48	3.1	5.289	54	27、通常》
2-4 - 39495-201-201	31	1 .	2.4	S 2250	-	< 5, <u>2</u> €1
% +1= ±3€ =401. =.		0.13	2:		. i ·	< 5.14)
gap 3mc 400 900 401	3.1	g.gt.	2.1	9 (1)	3.1	5 411
237-496 (43 -239-kumei-196-aimei-231-391	<u> </u>	2.		9-5-1		4. 5.12 5 1
200-301-400-300	7			• • i	180	1 _ y = 1

morber' means releviate diseaset 2... mg 40 1.1 mg MM 1.11 mg AM 1.11 mg AM 3.11 mg AM 3.11 mg AM. 1.10 mg 1.1. or 100 mg TED.

BEST POSSIBLE

Figure A.1 Patient's Global Assessment-OA/RA (protocol 024)

Figure 7. Patient's Global Assessment of Arthritic Condition: OA Patients (Study 024)

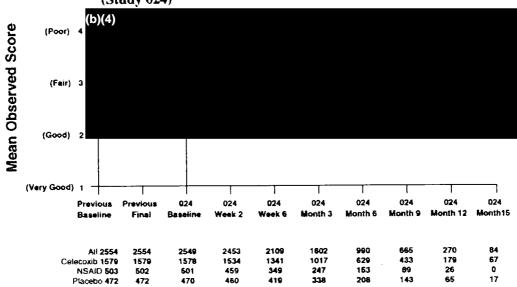


Figure 10. Patient's Global Assessment of Arthritic Condition: RA Patients (Study 024)

